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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/018,194	02/04/1998	BARBARA A. GILCHRIST	BU94-15A2	9447

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/02/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/018,194

Applicant(s)

GILCHREST ET AL.

Examiner

Sandra Wegert

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 20 September 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 and 11-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 February 1998 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Status of Application, Amendments, and/or Claims***

The Declaration of Dr. Gilcrest under 37 CFR 1.132, filed 23 April 2002 (Paper 18), has been entered.

The amendment filed 20 September 2002 (Paper No. 21) and the Amendment filed 23 April 2002 (Paper No. 19) have been entered. Claim 6 has been amended. Claims 1-5 and 11-52 were previously withdrawn by the examiner (6 November 2001, Paper 15). Claims 6-10 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Objections/Rejections***

#### ***Withdrawn Objections and/or Rejections***

##### ***Title***

The objection to the title as set forth at p. 4 of the previous Office Action (Paper No. 15, 6 November, 2001) is *withdrawn* in view of the amendment which introduced a new title (Paper No. 19, 11 April, 2002).

***Claim Objections***

The objection to Claims 8 and 10 for reciting non-elected inventions, as set forth at p. 4 of the previous Office Action (Paper No. 15, 6 November, 2001), is *withdrawn* in view of the explanation by the Applicant that Claims 8 and 10 do not encompass non-elected inventions (Paper No. 19, 11 April, 2002).

**Claim Rejections - 35 USC § 112, second paragraph-indefiniteness.**

The rejection of Claim 12 under 35 USC 112, second paragraph, for reciting the phrase "the pseudo-ligand" and "pseudo-pseudo-ligand" is *withdrawn*. The rejection was made as applied to Claim 8 (Paper 15, 6 November 2001), since that claim recited the phrases "the pseudo-ligand" and "pseudo-pseudo-ligand". However, as explained by the Applicant (Paper 19, 23 April 2002), claim 8 was amended to provide antecedent basis for "the pseudo-ligand" and to remove the phrase the "pseudo-pseudo-ligand."

**Maintained Objections and/or Rejections**

***35 U.S.C. § 112, first paragraph, Enablement.***

Claims 6-10 are rejected under 35 USC 112, first paragraph because the subject matter was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reasons for this rejection were set forth at pages 5-7 of the previous office action (Paper 15, 6 November 2001).

Briefly, the specification is not enabling for the limitations of the claims wherein prevention of apoptosis in epidermal keratinocytes is used as a method of inducing hair growth.

Claims 6-10 read on a method of inducing hair growth in a mammal by preventing apoptosis in keratinocytes. The claimed ligands to be used for the method of the invention are SEQ ID NO: 9 and the "KGA" fragment of SEQ ID NO: 9.

Applicants point out (Paper 19, 23 April 2002, p 6) that the Specification shows evidence that *KGA* peptides prevent loss of NIH-3T3 cells. Applicants also point to the binding experiments disclosed in which *KGA* binds to p75 (p. 47 of Specification), and to the experiments demonstrating that NGF rescues cultured keratinocytes that have been irradiated with UV light. The Applicants also take issue with the Examiner's assertion (in Paper 15, 6 November 2001) that "apoptosis of cultured keratinocytes caused by irradiation with UV light is a poor model of hair loss in a mammal" (Paper 19, 23 April 2002, p 6).

Despite Applicant's arguments, there is no enabling discussion or working examples disclosed in the instant application that: a) *NIH-3T3* fibroblasts, transfected to over-express p75, are related to keratinocytes or other cells found in a hair follicle; or, b) that fibroblast cell loss due to administration of amyloid is analogous to cell loss of keratinocytes of the hair follicle; or, c) that the *KGA* peptides recited in the claims use the same receptors and anti-apoptotic mechanisms as NGF (used for the method of rescuing keratinocytes, as disclosed in the Specification). As discussed in the previous Office Action (Paper 15, 6 November 2001) maintenance of hair growth in the skin of mammals involves a variety of interacting factors, including several types of cells in addition to keratinocytes, as well as immune factors and the influences of reproductive hormones (Christensen, Science News, **160**, 254, 2001). There are

also different mechanisms of hair maintenance and loss depending on the area of skin studied. Further illustration by the Applicants is necessary to explain how the disclosed method of keratinocyte cell death is related to mechanisms of follicular death in skin or how the disclosed experiments are related to inducing hair growth in mammalian skin.

The Declaration of Dr. Gilchrest, under 37 CFR 1.132, submitted 23 April 2002, demonstrates that the *KGA* peptide of SEQ ID NO: 9 caused a delay in hair follicles reaching later catagen stages, which the Applicant interprets as promoting the retention of hair. It includes statements which amount to an affirmation that the claimed subject matter functions as it was intended to function. This is not relevant to the issue of nonobviousness of the claimed subject matter and provides no objective evidence thereof. See MPEP § 716. It is unclear how catagen stage was measured, why anagen was not measured, or if this resulted in hair *growth*. More complete disclosure of the methods used would be useful in associating the disclosed experiments with inducing hair growth. For example, delaying maturation of hair follicles, which have been artificially "aged" with BDNF, is not similar to a method of inducing hair growth as claimed. Likewise, the journal articles submitted with the declaration under 37 CFR 1.132, do not provide enabling evidence for the claimed methods. The paper by Detmar, et al (1993, J. Invest. Dermatol., Supplement 101(1): 130s-134s) discusses the short lifespan of transplanted follicles – on the order of a few weeks- as well as the greater success seen in culturing several types of cells, including keratinocytes, digested from mammalian follicles. It is not clear how the Detmar, et al paper, by discussing the variety of cell cultures of keratinocytes and follicular matrix cells, contributes to enabling the Applicants' claimed methods of inducing hair growth. Similarly, the Paper by Moll (1995, J. Invest. Dermatol., 105(1): 14-21) showed

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that keratinocytes from several parts of the hair follicle can be maintained in culture, and not surprisingly, have different characteristics depending from which part of the follicle they were obtained. Although the Moll paper teaches that cells from different parts of the follicle have different characteristics and "ages" (see for example Figure 7), the paper does not contribute information that would serve to enable the claimed methods of the instant Application.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation required to determine how to use the disclosed polypeptides to cause hair growth in mammalian skin, the lack of direction or guidance in the specification regarding the same, the lack of working examples that measure hair growth, the state of the art which acknowledges the complexity of inducing new hair growth in mammalian skin, and the breadth of the claims which embrace methods of causing new hair growth in, for example, hairless skin --undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

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***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37



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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Elizabeth C. Kemmer*

SLW

11/25/02